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Meridian Bioscience, Inc. Inspired Science. Trusted Solutions.®	*illumigene*® Pertussis DNA Amplification Assay	
	Application Reference:	K133673
	Attachment Description:	Additional Information Request (January 13, 2014) **510(k) Summary**
	Application Date:	March 19, 2014

510(k) Summary

510(k) number: **K133673** **Date of Preparation: March 19, 2014**

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Trade Name:

illumigene® Pertussis DNA Amplification Assay
illumigene® Pertussis External Controls

Common Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay

Classification Name: Bordetella Pertussis DNA Assay System
(21 CFR 866.3980, Product Code OZZ)

Predicate Device: FilmArray® Respiratory Panel (RP), Catalog RFIT-ASY-001
K123620, K120267, K110764 and K103175,

Device Description:

The ***illumigene*** Molecular Diagnostic Test System is comprised of the ***illumigene***® Pertussis DNA Amplification Assay Test Kit, the ***illumigene***® Pertussis External Control Kit and the ***illumipro-10***™ Automated Isothermal Amplification and Detection System.

The ***illumigene*** Pertussis assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the presence of *Bordetella pertussis* in human nasopharyngeal swab specimens. Each ***illumigene*** Pertussis assay is completed using an ***illumigene*** Assay Control/Negative Control Reagent containing Control material, an ***illumigene*** Sample Buffer, an ***illumigene*** Pertussis Test Device and Mineral Oil. Nasopharyngeal swab specimens are eluted with ***illumigene*** Sample Buffer. The ***illumigene*** Assay Control Reagent is added to the eluted sample and heat-treated. Target and Control DNA are made available for isothermal amplification via heat-treatment. The heat-treated Specimen/Control sample is added to the ***illumigene*** Test Device. Mineral oil is added to the ***illumigene*** Test Device to prevent evaporation. DNA amplification occurs in the ***illumigene*** Test Device.

The ***illumipro-10*** heats each ***illumigene*** Pertussis Test Device containing prepared Sample and Control material, facilitating amplification of target DNA. When *B. pertussis* is present in the specimen, a 198 base pair sequence located within the IS481 insertional element of the *B. pertussis* genome is amplified and magnesium pyrophosphate is generated. Magnesium pyrophosphate forms a precipitate in the reaction mixture.

The ***illumipro-10*** monitors the absorbance characteristics of the reaction solutions at the assay Run Start ($Signal_{initial}$, S_i) and at the assay Run End ($Signal_{final}$, S_f). The ***illumipro-10***™ calculates the ratio of the Run End (Signal final or S_f) reads with the Run Start (Signal Initial or S_i) reads and compares the ratio to an established cut-off value. The ***illumipro-10*** performs this ratio calculation to both the TEST chamber and the CONTROL chamber.

Fixed cut-off values for the CONTROL chamber are used to determine validity. CONTROL chamber S_f:S_i ratios less than 90% are considered valid and allow for reporting of TEST chamber results (POSITIVE, NEGATIVE). CONTROL chamber S_f:S_i ratios greater than or equal to 90% are considered invalid. Results are reported as 'INVALID'; Test chamber results are not reported. More stringent cut-off criteria are applied to the Control chamber reaction to ensure amplification is not inhibited, reagents are performing as intended and that sample processing was performed appropriately.

Fixed cut-off values for the TEST chamber are used to report sample results. TEST chamber S_f:S_i ratios less than 82% are reported as 'POSITIVE'; TEST chamber S_f:S_i ratios greater than or equal to 82% are reported as 'NEGATIVE'. Numerical values are not reported.

The ***illumigene*** Pertussis External Control Kit contains a Positive Control Reagent. The ***illumigene*** Assay Control/Negative Control Reagent provided in the ***illumigene*** Pertussis kit serves as the External Negative Control Reagent. External Control reagents are provided to aid the user in detection of reagent deterioration, adverse environmental or test conditions, or variance in operator performance that may lead to test errors. External Control reagents are provided for use in routine Quality Control testing.

Intended Use:

The ***illumigene***® Pertussis DNA Amplification Assay, performed on the ***illumipro-10***™, is a qualitative in vitro diagnostic test for the direct detection of *Bordetella pertussis* in human nasopharyngeal swab samples taken from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis.*

The ***illumigene*** Pertussis assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Bordetella pertussis* by targeting the IS481 insertional element of the *Bordetella pertussis* genome. The IS481 insertional element can also be found in *Bordetella holmesii* and *Bordetella bronchiseptica* strains. Respiratory infection with *Bordetella pertussis, Bordetella holmesii* or *Bordetella bronchiseptica* may yield positive test results in IS481 assays. *B. holmesii* infection may cause clinical illness similar to *B. pertussis*, and mixed outbreaks involving both *B. pertussis* and *B. holmesii* infection have been reported. Additional testing should be performed if necessary to differentiate *B. holmesii* and *B. pertussis*. *B. bronchiseptica* is a rare cause of infection in humans. When clinical factors suggest that *B. pertussis* may not be the cause of respiratory infection, other clinically appropriate investigation(s) should be carried out in accordance with published guidelines.

Negative results for the ***illumi***gene Pertussis DNA Amplification Assay do not preclude *Bordetella pertussis* infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the ***illumigene*** Pertussis assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of *Bordetella pertussis* infection and should not be used as the sole basis for treatment or other patient management decisions.

illumigene Pertussis is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Predicate Device Comparison:

Similarities		
	DEVICE ***illumigene*® Pertussis**	**PREDICATE** **FilmArray® Respiratory Panel (RP) System** **Package Insert: RFIT-PRT-0011-02, May 2012**
Intended Use	Qualitative	Qualitative
Indications for Use	Professional Use	Professional Use
Assay Target	*Bordetella pertussis* IS481 Insertional Element	*Bordetella pertussis* DNA, promoter region of Toxin gene
Specimen Types	Nasopharyngeal Swab	Nasopharyngeal Swab
Detection	Self contained and automated	Self contained and automated

Differences		
	DEVICE ***illumigene*® Pertussis**	**PREDICATE** **FilmArray® Respiratory Panel (RP) System**
Test Format	DNA Amplification Assay; Loop-Mediated Isothermal Amplification (LAMP)	Multiplex PCR Amplification Assay
Reagents/Components	The ***illumigene*** Pertussis DNA Amplification Assay Kit contains ***illumigene*** Assay Control/Negative Control, ***illumigene*** Sample Buffer, ***illumigene*** Pertussis Test Device and Mineral Oil. External Positive Control materials are provided separately in the ***illumigene*** Pertussis External Control Kit. The ***illumigene*** Assay Control/Negative Control functions as the External Negative Control. The ***illumipro-10*** is provided separately.	The FilmArray Respiratory Panel (RP) Assay Kit contains FilmArray RP pouch, Sample Buffer, Hydration Solution, transfer pipettes and Sample Loading Syringes (with attached cannula). The FilmArray Instrument with Loading Station is provided separately.
External Controls	External Positive Control for the ***illumigene*** Pertussis Assay is provided in the ***illumigene*** Pertussis External Control Kit. The External Positive Control Reagent contains tris-buffered solution containing non-infectious Plasmid DNA (*B. pertussis* target DNA inserts) with azide (0.09%) as a preservative. The ***illumigene*** Assay Control/Negative Control provided in the ***illumigene*** Pertussis DNA Amplification Assay Kit functions as the External Negative Control. The Assay Control/Negative Control Reagent contains tris-buffered solution containing formalin-treated *E. coli* harboring non-infectious Plasmid DNA (*S. aureus* insert) with azide (0.09%) as a preservative.	The FilmArray Respiratory Panel (RP) Assay does not require external controls. External Controls are not providedfor the FilmArray Respiratory Panel (RP) Assay.
Amplification Technology and Target Sequence Detected	Assay performed with the ***illumipro-10***™ instrument, utilizes loop-mediated isothermal amplification (LAMP) technology for the detection of 198 base pair (bp) sequence of found in the IS481 Insertional Element of the the *Bordetella pertussis* genomeThe ***illumipro-10***™ detects changes in reaction solution absorbance by visible light transmission.	Assay performed with the FilmArray Instrument, utilizes freeze-dried reagents to perform nucleic acid purification reverse transcription, and nested multiplex PCR with DNA melt analysis for the detection of multiple respiratory pathogens along with a specific *B. pertussis* toxin DNA sequence..

Differences *(continued)*		
	DEVICE ***illumigene*® Pertussis**	**PREDICATE** **FilmArray® Respiratory Panel (RP) System**
Instrumentation	***illumipro-10™*** Automated Isothermal Amplification and Detection System	FilmArray® Instrument
Reading Method	Visible Light Transmission	Fluorescence Emissions
Interpretation of Results	Results of the ***illumigene*** Pertussis Assay are interpreted by the ***illumipro-10*** and reported as INVALID, POSITIVE and NEGATIVE based on change in light transmission of the reaction mixtures. EMPTY WELL is reported when an ***illumigene*** Test Device is not detected by the ***illumipro-10*** or when questionable Signal Initial (S_i) transmission is detected.	Results of the FilmArray Respiratory Panel (RP) Assay report are interpreted by the FilmArray Instrument for *B. pertussis* and reported as Detected, Not Detected or Invalid.
Performance Characteristics	**Prospective and Retrospective, All Comers** **Positive Percent Agreement (PPA):** **87.8 %** [95% CI: 75.8 - 94.3%] **Negative Percent Agreement (NPA):** **97.8%** [95% CI: 96.3 - 98.7%] **Retrospective Samples, Selected** **Positive Percent Agreement (PPA):** **90.5 %** [95% CI: 71.1 – 97.3%] **Negative Percent Agreement (NPA):** **87.5%** [95% CI: 64.0 – 96.5%]	**Prospective Samples** **PPA:** 100.0% [95% CI:54.1 - 100%] **NPA:** 99.9% [95% CI: 99.5 - 100%] **Retrospective Samples** **PPA:** 94.6% [95% CI: 85.1 - 98.9%] **NPA:** 96.5% [95% CI: 88.1 - 99.6%]

NON-CLINICAL PERFORMANCE DATA

Analytical Performance:

Precision/Reproducibility:

Blind coded panels of 10 samples were supplied to three independent laboratories. Samples were randomly sorted consisting of moderately positive (n=3), low positive (n=3), high negative (n=3) and negative (n=1) samples. Contrived moderately positive, low positive and high negative samples were prepared by inoculating simulated negative matrix (flocked nylon nasopharyngeal swabs inoculated with nasal wash) with *Bordetella pertussis* strain BAA-589, Tahoma I. A negative specimen containing no *Bordetella pertussis* was included in the study. Panel specimens were qualified for study use by replicate testing (n=20) for each of three production lots of ***illumigene*** Pertussis.

Testing was performed by at least two different operators at each site on the same day (intra-assay variability) for five days (inter-assay variability). Three lots of ***illumigene*** Pertussis and six ***illumipro-10*** instruments were used in this study. Positive and Negative Controls were tested with each panel. The results are given in the table below:

Sample Type	Clinical Site 1 Percent Agreement		Clinical Site 2 Percent Agreement		Clinical Site 4 Percent Agreement		Total					
							Percent Agreement		Average S_T:S_I	SD	%CV	95% CI
Moderate Positive	30/30	100.0	30/30	100.0	30/30	100.00	90/90	100.0	57.51	4.14	7.20%	95.9 – 100.0
Low Positive.	27/30	90.0	29/30	96.7	30/30	100.0	86/90	95.6	58.16	10.02	17.23%	89.1 – 98.3
High Negative	26/30	86.7	23/30	76.7	29/30	96.7	78/90	86.7	96.19	11.47	11.92%	78.1 – 92.2
Negative	10/10	100.0	9/10	90.0	10/10	100.0	29/30	96.7	100.29	4.75	4.73%	83.3 – 99.4
Positive Control	10/10	100.0	10/10	100.0	10/10	100.0	30/30	100.0	56.83	4.83	8.50%	88.6 - 100.0
Negative Control	10/10	100.0	10/10	100.0	10/10	100.0	30/30	100.0	100.70	3.04	3.01%	88.6 - 100.0

Detection limit:

Analytical Sensitivity studies were designed to determine, within 95% confidence intervals, the analytical limit of detection (LoD) of *Bordetella pertussis*. The LoD is the lowest number of colony-forming units (CFUs) per test aliquot that can be distinguished from negative samples with a high degree of probability (95%). *Bordetella pertussis* strain BAA-589 was evaluated for analytical Limit of Detection. Culture confirmed stock concentrations were standardized and subsequently diluted serially into sterile saline. Dilutions were combined with simulated negative matrix (flocked nylon swabs inoculated with nasal wash screened negative for *B. pertussis)* prior to test; Meridian utilized a simulated negative matrix for all analytical studies.

Each dilution evaluated in the ***illumigene*** Pertussis assay used individually prepared replicates. Not all prepared dilutions were tested in the ***illumigene*** Pertussis assay; testing for select dilutions was discontinued when replicate testing did not meet criteria established for limit of detection (e.g. more than 1 negative replicate obtained). The lowest dilution producing positive results in at least 19 of 20 replicates was identified as the preliminary assay limit of detection. Once a preliminary LoD concentration was established, an additional 60 replicates were evaluated by two different technicians to confirm the final LoD concentration for each kit lot.

Testing was performed using three lots of ***illumigene*** Pertussis and six ***illumipro-10*** instruments. External Positive and Negative Controls were tested daily. The Limit of Detection for the assay was reported as 1.48 CFU/Test or 3265 CFU/mL).

The following *B. pertussis* strains were tested and produced positive reactions at the stated assay limit of detect of 1.48 CFU/Test (3265 CFU/mL) with ***illumigene*** Pertussis: ATCC 12743, ATCC 8478, ATCC 8467, ATCC 9797, ATCC 53894, ATCC 10380, ATCC 12742, and A639. The following *B. pertussis* strains were tested and produced positive reactions at 1.59 CFU/Test or 3500 CFU/mL) with ***illumigene*** Pertussis: ATCC 51445 and ATCC BAA-1335.

Analytical specificity:

Interference Testing:

Interfering substance testing was performed to assess the potential impact of non-microbial contaminants expected to be present in samples collected for *Bordetella pertussis* testing on ***illumigene*** Pertussis test results. Potentially interfering substances were tested with simulated negative and contrived positive (*B. pertussis* strain BAA-589) nasopharyngeal swab samples. Potentially interfering substances were added to eluted simulated negative and contrived positive swab samples in Tris EDTA at final concentrations of 0.1 mg/mL, 1% v/v, 1% w/v, or greater and tested. Dilution Controls were prepared by adding a sterile saline solution in place of the potentially interfering substance.

The following biological substances, at the saturated solvent/diluents concentrations indicated do not interfere with the ***illumigene*** Pertussis test results: Mucin (1% w/v), Human DNA (200 ng/µL), Whole blood (1% w/v).

The following chemical substances, at the saturated solvent/diluents concentrations indicated do not interfere with test results: Acetaminophen (10 mg/mL), Advil® [Ibuprofen (10 mg/mL)], Afrin® Decongestant Nasal Spray [Oxymetazoline hydrochloride (0.0005% w/v)], Albuterol Sulfate [Salbutamol sulfate (1% w/v)], Aspirin (5 mg/mL), Coricidin® HBP Cold/Flu tablets [Acetominophen (3.26 mg/mL), Chlorpheniramine maleate (0.02 mg/mL)], Diphenhydramine HCl (0.25 mg/mL) , Erythromycin (2% w/v), Mupirocin (2% w/v), Petroleum Jelly [White Petrolatum (1% w/v)], Robitussin® Cough+Chest Congestion DM Cough Syrup [Dextromethorphan HBr (0.1 mg/mL), Guaifenesin (1.0 mg/mL)], Suphedrine PE [Phenylephrine HCl (0.3 mg/mL)], Saline Nasal Spray [Sodium chloride (0.0065% w/v)], Smokeless Tobacco (snuff) (1% w/v), Tobramycin (0.6 mg/mL), Vicks® VaporRub® [Camphor (0.48% w/v), Eucalyptus oil (0.12% w/v), Menthol (0.26% w/v)].

Ibuprofen (10 mg/mL) produced invalid results (3/6 replicates) during original testing of contrived *B. pertussis* specimens. All repeat testing produced positive results (10/10

replicates). As the original results were not confirmed, Ibuprofen (10 mg/mL) is not considered an interfering substance.

Aspirin was found to interfere with ***illumi****gene* Pertussis testing at concentrations above 5 mg/mL.

Cross-Reactivity Study:

Potentially cross-reacting microorganisms expected to be present in nasopharyngeal swab specimens were added to negative and contrived positive samples. Negative samples were prepared with flocked nylon nasopharyngeal swabs inoculated with confirmed negative nasal wash. The contrived positive sample was prepared by spiking confirmed negative sample matrix (flocked nylon nasopharyngeal swabs inoculated with nasal wash) with *Bordetella pertussis* strain BAA-589, at concentrations at or around the determined limit of detection. Dilution Controls were prepared by adding a sterile saline solution in place of the potentially cross-reactive organisms. Each inoculated sample was tested in triplicate.

Potentially cross-reactive microorganisms were at minimum concentrations of 1.0×10^6 CFU/mL for bacteria/fungi or concentrations greater than 1.0×10^5 $TCID_{50}$/mL for viruses.

None of the following organisms reacted with ***illumi****gene* Pertussis:
Acinetobacter baumannii, Acinetobacter calcoaceticus, Acinetobacter lwoffii, Actinomyces odontolyticus, Arcanobacterium haemolyticum, Bacillus subtilis, Bacteroides fragilis, Bordetella avium, Bordetella hinzii, Bordetella parapertussis, Bordetella petrii, Bordetella trematum, Burkholderia cepacia, Candida albicans, Candida glabrata, Chlamydia pneumoniae, Chlamydia trachomatis, Citrobacter freundii, Clostridium difficile, Corynebacterium diphtheriae, Corynebacterium pseudodiphtheriticum, Enterobacter cloacae, Enterococcus faecalis, Escherichia coli, Escherichia coli (ESBL), *Fusobacterium nucleatum, Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae* (KPC), *Lactobacillus acidophilus, Lactobacillus plantarum, Legionella jordanis, Legionella longbeachae, Legionella micdadei, Legionella pneumophila, Listeria monocytogenes, Moraxella catarrhalis, Mycobacterium tuberculosis, Mycoplasma genitalium, Mycoplasma hominis, Mycoplasma pneumoniae, Neisseria cinerea, Neisseria elongata, Neisseria gonorrhoeae, Neisseria meningitidis, Nocardia asteroides, Peptostreptococcus anaerobius, Proteus mirabilis, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Serratia liquefaciens, Staphylococcus aureus, Staphylococcus epidermidis, Stenotrophomonas maltophilia, Streptococcus anginosus* (Group F), *Streptococcus bovis* (Group D), *Streptococcus canis* (Group G), *Streptococcus dysgalactiae ssp. dysgalactiae, Streptococcus dysgalactiae ssp. equisimilis Streptococcus intermedius, Streptococcus mitis, Streptococcus mutans, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus salivarius, Streptococcus suis, Ureaplasma urealyticum*, Adenovirus,

Coronavirus, Coxsackievirus, Cytomegalovirus, Epstein Barr Virus, Herpes Simplex Virus 1, Herpes Simplex Virus 2, Human Metapneumovirus, Influenza A, Influenza B, Measles virus, Mumps virus, Parainfluenza virus 1, Parainfluenza virus 2, Parainfluenza virus 3, Respiratory syncytial virus A, Respiratory syncytial virus B, Rhinovirus.

Bordetella holmesii and *Bordetella bronchiseptica* also contain the IS481 insertional element. *Bordetella bronchiseptica* ATCC® Strain 4617 and *Bordetella holmesii* were tested at 1.0×10^6 CFU/mL and found to react with the ***illumigene*** Pertussis assay.

Unexpected results were observed during original testing of specimens containing *B. hinzii*, *H. parainfluenzae* and *M. genitalium*. One of three negative sample replicates containing *B. hinzii* produced a false-positive result that was not confirmed with further testing (20/20 replicates). Three of three negative sample replicates containing *H. parainfluenzae* produced false-positive results that were not confirmed with further testing (20/20 replicates). Three of three *B. pertussis* positive sample replicates produced invalid results that were not confirmed with further testing (10/10 replicates). Three of three negative sample replicates containing *M. genitalium* produced invalid results that were not confirmed with further testing (10/10 replicates). As repeat testing using a heightened number of replicates did not confirm original results, *B. hinzii*, *H. parainfluenzae* and *M. genitalium* are not considered cross-reactive or interferents in ***illumigene*** Pertussis testing.

Assay cut-off:

The ***illumigene*** Pertussis assay is manufactured with fixed cut-off values. The product is designed around a pre-selected cut-off value and amplification reagent concentrations are optimized to ensure appropriate reactions are obtained. Development optimization includes evaluation of characterized positive and negative clinical specimens. Amplification reagent concentrations are adjusted during design as needed to ensure ***illumigene*** results are aligned with clinical specimen reported results.

Cut-off values applied in the following manner:

- The ***illumipro-10***™ calculates the ratio of the Run End (Signal final or S_f) reads with the Run Start (Signal Initial or S_i) reads and compares the ratio to an established cut-off value. The ***illumipro-10*** performs this ratio calculation to both the TEST chamber and the CONTROL chamber.
- Fixed cut-off values for the CONTROL chamber are used to determine validity. CONTROL chamber S_f:S_i ratios less than 90% are considered valid and allow for reporting of TEST chamber results (POSITIVE, NEGATIVE). CONTROL chamber S_f:S_i ratios greater than or equal to 90% are considered invalid. Results are reported as 'INVALID'; Test chamber results are not reported. More stringent cut-off criteria are applied to the Control chamber reaction to ensure amplification is not inhibited, reagents are performing as intended and that sample processing was performed appropriately.

Fixed cut-off values for the TEST chamber are used to report sample results. TEST chamber S_f:S_i ratios less than 82% are reported as 'POSITIVE'; TEST chamber S_f:S_i ratios greater than or equal to 82% are reported as 'NEGATIVE'. Numerical values are not reported.

CLINICAL PERFORMANCE DATA:

Clinical Studies:

Clinical Performance:

Clinical trials for the ***illumigene*** Pertussis DNA Amplification Assay, including the ***illumipro-10*** Automated Isothermal amplification and detection system, were conducted from December 2012 to July 2013. A total of 729 qualified nasopharyngeal (NP) swab specimens collected from patients suspected of having *Bordetella pertussis* infection were evaluated with the test. All specimens were leftover and de-identified.

Performance characteristics of the assay were determined by comparison to a Composite Comparator Reference Method that included two manufacturer validated, real-time PCR Assays (PCR1 and PCR2) followed by bi-directional sequencing. Both comparator PCR assays targeted unique sequences within the IS481 insertional element; neither of the comparator target sequences overlaps with the ***illumigene*** Pertussis assay target sequence. Specimens producing positive *Bordetella pertussis* results from either comparator PCR assay were sent for bi-directional sequencing. Only samples that matched sequences within the *Bordetella pertussis* genome with pre-defined quality scores (PHRED20 and E-values) were considered true positives. Samples were considered negative when neither comparator PCR assay returned positive *Bordetella pertussis* results.

The clinical study population included retrospective and prospective specimens. A total of 508 (69.7%) prospective and 221 (30.3%) retrospective specimens were tested and included in final performance calculations. The retrospective sample population included non-selected specimens (all comers) and selected specimens. Overall performance characteristics of ***illumigene*** Pertussis Assay are summarized in Table 1.

Table 1. *illumigene* Assay Performance

Specimen Description	Positive Specimens			Negative Specimens			Invalid Results[b]
	illumigene vs. Comparator	PPA[a]	95% CI	*illumigene* vs. Comparator	NPA	95% CI	
Composite Method Comparator, All Comers							
Prospective	39/45	86.7%	73.8 - 93.7%	447/459	97.4%	95.5 – 98.5%	2 (13)
Retrospective	4/4	100.0%	51.0 - 100.0%	176/178	98.9%	96.0 – 99.7%	0
Total:	**43/49**	**87.8%**	**75.8 – 94.3%**	**623/637**	**97.8%**	**96.3 – 98.7%**	**2 (13)**
Composite Method Comparator, Selected Specimens							
Retrospective	19/21	**90.5%**	71.1 – 97.3%	14/16	**87.5%**	64.0 – 96.5%	0

[a] *Eight specimens produced false-negative **illumigene** results when compared to the Composite Comparator Method. Six of the eight specimens produced detectable levels of DNA between 35 and 40 comparator assay amplification cycles and were confirmed positive by bi-directional sequencing. Three of these six specimens gave positive results in only one of the two comparator PCR/Sequencing assays.*

[b] *11/13 initial invalid specimens produced valid results upon repeat testing.*

False-negative ***illumigene*** results were individually evaluated at the conclusion of clinical testing. The Cycle threshold (Ct) values produced during comparator assay testing were above 35 for one or both PCR/Bi-directional sequencing assays for six of the eight specimens evaluated. High Ct values in PCR assays may indicate that low levels of DNA are present. False-negative ***illumigene*** results and corresponding Composite Comparator data are shown in Table 2.

Table 2. False-Negative *illumigene* Specimens, Comparator Assay Results

Specimen Designation	Specimen Status	PCR1		PCR2	
		Ct Value	Bi-Directional Sequencing Result	Ct Value	Bi-Directional Sequencing Result
1-19	**Prospective**	**34.90**	**+**	**33.85**	**+**
1-29	Prospective	Negative	N/A	37.69	+
1-259	**Prospective**	**34.07**	**+**	**35.09**	**+**
1-269	Prospective	35.72	+	Negative	N/A
1-275	Prospective	Negative	N/A	39.13	+
3-33	Prospective	39.28	+	35.80	+
4-710	Retrospective	36.87	+	36.06	+
4-712	Retrospective	37.44	+	38.41	+

Four independent clinical test sites located in the Midwestern, Northern, Southern, and Eastern regions of the United States participated in the device evaluation All samples included in the study were submitted to the testing laboratory by an ordering physician

for *Bordetella pertussis* testing and were presumed from symptomatic patients. No restrictions were placed on age, gender, medications or known pharmaceutical therapies.

Clinical studies were conducted with multiple nasopharyngeal swab and sample elution buffer types. Sample buffers tested during clinical studies included 0.85 % Saline (n=30 or 4.1%), Tris EDTA (n=8 or 1.1%) and Molecular Grade Water (n=687 or 94.2%). All sample buffers were used in 0.5 mL volumes. Analytical studies were performed with 0.85% Saline, Tris EDTA, Phosphate Buffered Saline (PBS) and Molecular Grade Water. Analytical studies established equivalence between all sample elution buffer types.

Clinical performance data was evaluated by patient age and gender. Age information was known for 723 (99.2%) of the patients from whom samples were tested. Patient age ranged from 1 month to 88 years. Thirty-eight (5.2%) patients were less than 1 year of age; 13 (1.8%) were between 1 and 2 years old; 296 (40.6%) were between 2 and up to 12 years, 157 (21.5%) were between 12 and up to 21 years, 190 (26.0%) were above 21 but below 65 years, and the remaining 29 (4.0%) patients were above 65 years of age. The study population included 413 (56.7%) female and 308 (42.2%) male patients. Gender was unknown for 8 (1/1%) patients included in the study. There is no expectation that the ***illumigene*** Pertussis assay performance characteristics are influenced by patient gender.

Performance data by Clinical Test Site, analyzed based on the Composite Reference Method, is shown in Table 3. Statistical analysis of Site performance data was performed with no significant difference among Sites identified.

Table 3. *illumigene* Pertussis Assay Performance by Clinical Test Site, Composite Reference Method (CRM)

Specimen Description	Positive Specimens			Negative Specimens			Invalid Results
	illumigene vs. Comparator	PPA	95% CI	*illumigene* vs. Comparator	NPA	95% CI	
Composite Method Comparator, All Comers							
Site 1	35/40	**87.5%**	73.9 – 94.5%	440/450	**97.8%**	96.0 – 98.8%	2 (13)
Site 2	4/4	**100.0%**	51.0 – 100.0%	67/69	**97.1%**	90.0 – 99.2%	0 (2)
Site 3	0/1	**0.0%**	0.0 – 79.3%	7/7	**100.0%**	64.6 – 100.0%	0 (0)
Site 4	4/4	**100.0**	51.0 – 100.0%	109/111	**98.2%**	93.7 – 99.5%	0 (0)
Composite Method Comparator, Selected Specimens							
Site 1	**15/15**	**100.0%**	79.6 - 100.0%	**6/8**	**75.0%**	40.9 – 92.9%	0 (0)
Site 4	**4/6**	**66.7%**	30.0 – 90.3%	**8/8**	**100.0%**	67.6 – 100.0%	0 (0)

Expected values/Reference Range:

Overall incidence of *B. pertussis* as detected by the ***illumigene*** Pertussis Assay in prospectively and retrospectively collected, non-selected specimens (all comers) during the period of this study was 8.2% (57/692).

CONCLUSIONS

The ***illumigene***® Pertussis DNA amplification assay, performed on the ***illumipro-10***™, can be used to detect *Bordetella pertussis* in human nasopharyngeal swabs obtained from patients suspected of having respiratory infection attributable to *Bordetella pertussis.*

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 25, 2014

MERIDIAN BIOSCIENCE, INC.
MICHELLE SMITH
SR. DIRECTOR REGULATORY AFFAIRS AND DESIGN ASSURANCE
3471 RIVER HILLS DRIVE
CINCINNATI, OH 45244

Re: K133673
Trade/Device Name: *illumigene* Pertussis DNA Amplification Assay
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: II
Product Code: OZZ
Dated: March 13, 2014
Received: March 19, 2014

Dear Ms. Smith:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

John Hobson -S for

Sally Hojvat, M.Sc., Ph.D
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*

K133673

Device Name

illumigene® Pertussis DNA Amplification Assay

Indications for Use *(Describe)*

The ***illumigene®*** Pertussis DNA Amplification Assay, performed on the ***illumipro-10™***, is a qualitative in vitro diagnostic test for the direct detection of *Bordetella pertussis* in human nasopharyngeal swab samples taken from patients suspected of having respiratory tract infection attributable to *Bordetella pertussis*.

The ***illumigene*** Pertussis assay utilizes loop-mediated isothermal DNA amplification (LAMP) technology to detect *Bordetella pertussis* by targeting the IS481 insertional element of the *Bordetella pertussis* genome. The IS481 insertional element can also be found in *Bordetella holmesii* and *Bordetella bronchiseptica* strains. Respiratory infection with *Bordetella pertussis*, *Bordetella holmesii* or *Bordetella bronchiseptica* may yield positive test results in IS481 assays. *B. holmesii* infection may cause clinical illness similar to *B. pertussis*, and mixed outbreaks involving both *B. pertussis* and *B. holmesii* infection have been reported. Additional testing should be performed if necessary to differentiate *B. holmesii* and *B. pertussis*. *B. bronchiseptica* is a rare cause of infection in humans. When clinical factors suggest that *B. pertussis* may not be the cause of respiratory infection, other clinically appropriate investigation(s) should be carried out in accordance with published guidelines.

Negative results for the ***illumi***gene Pertussis DNA Amplification Assay do not preclude *Bordetella pertussis* infection and positive results do not rule out co-infection with other respiratory pathogens. Results from the ***illumigene*** Pertussis assay should be used in conjunction with information obtained during the patient's clinical evaluation as an aid in diagnosis of *Bordetella pertussis* infection and should not be used as the sole basis for treatment or other patient management decisions.

illumigene Pertussis is intended for use in hospital, reference or state laboratory settings. The device is not intended for point-of-care use.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

John Hobson -S
2014.03.24 11:49:51 -04'00'

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